Vancomycin-Resistant Enterococci Infections in the Department of Defense: Annual Report 2013

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Vancomycin-resistant Enterococci (VRE) are Gram-positive cocci that are resistant to vancomycin and most commonly infect seriously ill patients that have prolonged hospital stays or antibiotic use. Hospital acquired VRE infections are associated with high rates of morbidity and mortality and are a concern for hospitals around the world. The objective of this annual retrospective report is to summarize the VRE infection burden in the Department of Defense (DOD) and the Department of the Navy (DON) for calendar year (CY) 2013. This summary includes demographic and clinical characteristics, antibiotic susceptibility patterns, prescription practices, and HAI metrics for all DOD and DON beneficiaries. Overall, the incidence rates of VRE in the general US population, the DOD and DON are decreasing. No substantial changes in VRE risk groups were seen for 2013 as VRE continues to affect elderly females and manifest as urinary tract infections. In addition, no substantial changes in antibiotic susceptibility were seen in 2013. Linezolid, gentamicin and streptomycin remain viable treatments for VRE. Although current infection control practices seem to be decreasing the overall burden of VRE, healthcare associated infections are still a major problem for transmission of VRE in the DOD and the DON. Better infection control practices need to be introduced to help control healthcare associated infections.

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Abstract

Vancomycin-resistant *Enterococci* (VRE) are Gram-positive cocci that are resistant to vancomycin and most commonly infect seriously ill patients that have prolonged hospital stays or antibiotic use. Hospital acquired VRE infections are associated with high rates of morbidity and mortality and are a concern for hospitals around the world. The objective of this annual retrospective report is to summarize the VRE infection burden in the Department of Defense (DOD) and the Department of the Navy (DON) for calendar year (CY) 2013. This summary includes demographic and clinical characteristics, antibiotic susceptibility patterns, prescription practices, and healthcare-associated (HA) infection metrics for all DOD and DON beneficiaries. Overall, the incidence rates of VRE infections in the general United States (US), DOD, and DON populations are decreasing. VRE risk groups did not substantially change in 2013 as VRE continues to predominately affect elderly females and manifest as urinary tract infections (UTIs). In addition, antibiotic susceptibility patterns did not substantially change in 2013. Linezolid, gentamicin, and streptomycin remain viable treatments for VRE. Although current infection control practices seem to be decreasing the overall burden of VRE, HA infections are still a major problem for transmission of VRE in the DOD and the DON. Improved infection control practices would help to minimize the spread of these infections.

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Executive Summary

The EpiData Center Department (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) conducts routine surveillance of clinically significant outcomes within the DON, as DOD. This report provides a summary of the VRE infection burden in the DON and DOD for calendar year 2013.

Positive *Enterococcus* isolates were identified utilizing the Health Level 7 (HL7) formatted microbiology data. Current rates of VRE infections were compared to previous years and the historic mean rate of infection among the DON and DOD. VRE infection rates were also compared by demographic and clinical characteristics to determine at-risk populations.

Overall, the incidence rates of VRE infections in the general US, DOD, and DON populations are decreasing. VRE risk groups did not substantially change in 2013 as VRE continues to predominately affect elderly females and manifest as UTIs. In addition, antibiotic susceptibility patterns did not substantially change in 2013. Linezolid, gentamicin, and streptomycin remain viable treatments for VRE.

Although this report indicates that current infection control practices seem to be decreasing the overall burden of VRE, healthcare-associated infections are still a major problem in the transmission of VRE in the DOD and the DON. Introduction of better infection control practices should help control healthcare associated infections.

Introduction

Enterococci are Gram-positive cocci that are normal inhabitants of the human gut, and typically do not cause infection unless the host has a suppressed or compromised immune system.[1] *Enterococcus* infections commonly manifest as UTIs, intra-abdominal cavity infections, and blood stream infections (BSIs).[2-4] A VRE species is any member of the *Enterococcus* genus that is resistant to vancomycin, a glycopeptide antibiotic.[1] *Enterococcus faecium* and *E. faecalis* are the species most commonly associated with VRE infections, though studies have identified *E. raffinosus* as the species with highest rates of resistance.[5,6] Experts hypothesize that resistance genes developed due to selective pressure caused by a drastic increase in the use of vancomycin during the 1980s and 1990s. This increased use was in response to another multi-drug resistant organism (MDRO), methicillin-resistant *Staphylococcus aureus* (MRSA), as well as the common use of prophylactic vancomycin for surgical and indwelling catheter patients.[7] Research has identified varying resistance patterns among VRE strains caused by resistant genes passed between organisms.

VRE initially emerged in 1987 in Europe. Within a decade of identification, it spread and became a pathogen of concern in US hospitals, exhibiting resistance to multiple antibiotics and causing a wide range of infections with high mortality.[2] Mortality rates in patients with VRE bacteremia may reach up to 70.0%.[8] In 1992, 4.4% of US *Enterococcus* isolates were resistant to vancomycin, and the rate of nosocomial spread of VRE increased from 0.3% in 1989 to 7.9% in 1993; by 1995, the healthcare community reported pockets of endemicity.[1,2,9] By 1997, VRE was the second most common HA infection, linked to approximately 12.0% of all HA infections, and by 1999, VRE was associated with 17.0% of all HA infectionss.[10] After 1999, the rate of VRE incidence began to decrease, most likely as a result of the implementation of recommended infection control techniques from the Hospital Infection Control Practices Advisory Committee (HICPAC).[1]

However, current trends demonstrate that VRE infections are rising once again. One US study reported hospitalizations due to VRE infections increased from 3.2 per 10,000 hospitalizations to 6.5 per 10,000 total hospitalizations from 2003-2006.[11] Some European countries have also documented increasing rates of VRE infections, with vancomycin resistance reportedly as high as 28.0% among *E. faecium* isolates.[12] Experts believe that the widespread use of vancomycin to treat MRSA is an important reason behind the emergence, continued spread, and increasing trend of VRE infections in the US.[13]

There is a drastic difference between the virulence of European and US VRE strains, however. European VRE strains are frequently more benign and exist in a community reservoir; HA infections are not common.[3] Such a community reservoir does not exist in the US, where VRE HA infections have a higher rate of morbidity and mortality.[3] In the US, the major reservoir for VRE are hospitalized patients with gastrointestinal carriage of VRE.[8] Research supports the idea that VRE can be spread by direct person-to-person contact, including carriage on the hands of healthcare personnel, contaminated environmental surfaces, or patient care equipment.[8]

VRE infections tend to occur in seriously ill, hospitalized patients, especially among patients with prolonged hospital stays and patients who recently received organ transplants.[8] It is likely that vancomycin use predisposes patients to colonization and infection with VRE by inhibiting the growth of the normal Gram-positive intestinal flora and providing a selective advantage for VRE that may be present in small numbers in the individual's bowel.[8] Other risk factors for VRE infection include previous use of third generation cephalosporins, to which enterococci are intrinsically resistant; advanced age; severity of underlying condition; prior HA infection; pressure sores; and recent intra-abdominal surgery.[14-16]

HICPAC recommends prudent use of vancomycin, education of the hospital staff about VRE, effective use of the microbiology laboratory, and implementation of standard contact precaution protocols, such as isolation of infected patients and proper use of gloves and gowns, as ways to control transmission of VRE in hospitals.[8] Multiple studies show the positive impact that active surveillance of high-risk patients has on reducing the number of VRE infections in the healthcare setting.[17] One study in particular showed that active surveillance and contact precautions prevented VRE infections in an intensive care unit (ICU) in which 100% of the patients were colonized with VRE.[17]

Treatment for enterococcal infections normally includes an aminoglycoside plus another cell-wall active agent (β-lactam antibiotic). This is problematic for VRE infections, however, as they are often resistant to many, if not all, of these antibiotics, leaving few treatment options.[10] For patients allergic to penicillin or who have ampicillin- or penicillin-resistant strains, clinicians highly recommend vancomycin used in combination with other antibiotics, including aminoglycosides.[8] Quinupristin/dalfopristin was the first antibiotic developed for VRE. This antibiotic is only meant for treatment of *E. faecium*, as other *Enterococcus* isolates are intrinsically resistant to it. Since research identified that the use of quinupristin/dalfopristin was associated with debilitating adverse events, it has not been widely used since 2001.[18] Linezolid, an oxazolidinone developed in 2000, is another relatively new first line antibiotic and is effective against *E. faecium* and several other *Enterococcus* species. Some resistance has already been reported for linezolid.[18] Resistance has also been documented with daptomycin, which was developed in 2003 and is another treatment option for Gram-positive bacterial infections.[18] Fluoroquinolones are not highly recommended to treat VRE infections, as there are other classes of antibiotics that are more effective in clearing infection. However, fluoroquinolones are quite effective in the treatment of UTIs.[8]

The objective of this annual retrospective report is to summarize the VRE infection burden in the DOD and the DON for calendar year (CY) 2013. This summary includes demographic and clinical characteristics, antibiotic susceptibility patterns, prescription practices, and HAI metrics for all DOD and DON beneficiaries.

Methods

Positive cultures for *Enterococcus* were identified from microbiology data in Health Level 7 (HL7) format that originated from fixed military treatment facilities (MTFs). Any *Enterococcus* species isolate resistant to vancomycin was considered a VRE isolate. BacLink and WHONET software programs, which were developed by the World Health Organization (WHO) to aid in the identification and analysis of MDROs, were used to identify VRE isolates and organize antibiotic susceptibilities within microbiology records.[19] VRE prevalence cases were defined as unique VRE isolates per person per calendar month. VRE incidence was defined as the first unique VRE isolate per person per calendar year. Surveillance cultures for VRE, which include all rectal swabs, were excluded from this analysis, as surveillance cultures are usually indicative of colonization and not true infection.

Demographics were described using variables within the HL7 microbiology records. The TRICARE region was defined by the region of the servicing MTF, identified by the requesting Defense Medical Information System (DMIS) identification number. Age was defined as patient age at the date of specimen collection using date of birth. Sponsor service (Air Force, Army, Marine Corps, and Navy only) and beneficiary status (Active Duty, Recruit, Retired, Family Member, and Other) were identified by the patient category code. The Family Member beneficiary category included family members of active duty service members and retirees; all other family members and beneficiaries (including National Guard members, reservists, and civilians) were given the beneficiary category designation of Other.

Clinical characteristics were also described using variables within the HL7 microbiology records. Encounter type was defined by the first letter of the four-letter Medical Expense and Performance Reporting System (MEPRS) code, with "A" indicating an inpatient encounter and all other codes grouped as outpatient encounters. Specimen sources and body site fields were used to categorize isolates into the following infection types: urinary tract, blood stream, gastrointestinal tract, skin and soft tissue, respiratory, sterile, and other. To classify surgical VRE infections, the HL7 microbiology records indicating a VRE infection were linked to the Standard Inpatient Data Record (SIDR) database using a unique identifier. The International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes found in the SIDR records were used to classify a specimen as surgical. Only intra-abdominal surgeries are a significant risk factor for a surgical site acquisition of VRE, therefore, only intra-abdominal procedures were considered in defining the surgery infection type.[15,16] Surgery was defined using the 2013 National Healthcare Safety Network's (NHSN) ICD-9-CM code listing of intra-abdominal surgeries.[20]

The antibiotic susceptibility test results from the microbiology records were used to create an antibiogram. The first VRE isolate per patient per year was included. The antibiotics included in the antibiogram were based on the Clinical and Laboratory Standards Institute (CLSI) testing guidelines for *Enterococcus* species isolates.[21] The Cochran-Armitage test was used to examine trend across the surveillance period.

Hospitalization records from the SIDR database were also used to examine VRE exposure and infection burden metrics within the MTFs. Infections were classified as hospital-onset (HO),

healthcare-associated (HA), or community-onset (CO) VRE infections. A patient was considered to have an HO VRE infection if the specimen collection date was between the patient's admission and discharge dates and at least three days following the admission date. An infection was considered to be HA if an inpatient encounter occurred within the 12 months prior to the current specimen collection date, indicating recent exposure to the hospital environment. Other factors commonly used to define HA infections, such as the presence of an invasive device at the time of infection, patient history of surgery or dialysis, or residence in a long-term care facility, were not used to further define HA infections due to lack of data.[22] All outpatient encounters with a positive VRE culture were considered to be CO. Individuals who had a specimen collection date within three days from the admission date and no documentation of an inpatient encounter within the 12 months prior to the current specimen collection date were also considered to be CO.[22]

Seven HAI metrics were used in this analysis, including metrics for admissions prevalence, overall prevalence, HO bacteremia, HO UTIs, surgical site infections (SSIs), central line-associated bloodstream infections (CLABSIs), and ventilator-associated pneumonia (VAP). These were based on the National Healthcare Safety Network (NHSN) guidelines and HICPAC position paper on recommended metrics for MDROs.[22,23] The admissions prevalence metric measured the magnitude of VRE imported into fixed DOD MTFs, and the overall prevalence metric measured the magnitude of a patient's exposure in the healthcare setting to other patients with VRE. For the infection burden metrics, only the first HO VRE isolate per patient per admission was selected. Table 1 presents the classification for each metric.

Table 1. Classification of Infection Burden Metric Parameters

Metric	Definition
Overall prevalence	Any record where VRE was isolated from specimen collected at least three days after admission
Admissions prevalence	Any record where VRE was isolated from specimen collected within the first three days of admission
Hosptial onset bacteremia	Any record with body site or specimen source of blood that was collected at least three days after admission
Hospital onset urinary tract infections	Any record with body site or specimen source of urine that was collected at least three days after admission
Surgical site infections	Any record following NHSN operative procedure groupings[20]; The procedure is within admission and discharge dates; AND Infection occurs within 30 days of the procedure
Central line-associated bloodstream infections	Any record with body site or specimen source of blood; Records with ICD-9-CM procedure codes: 38.91, 38.92, 38.93, or 38.97; AND Specimen was collected at least three days after admission
Ventilator-associated pneumonia	Any record with body site or specimen source of respiratory sample; Records with ICD-9-CM procedure codes: 96.7, 96.04, 96.71, or 96.72; AND Specimen was collected at least three days after admission

Records are from linked Health Level 7 (HL7) microbiology data and the Standard Inpatient Data Record (SIDR).
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 4 February 2014.

Overall prevalence and admissions prevalence denominators were calculated using the total number of hospital admissions per year.[21] For the surveillance period, average rates were calculated and, because variability was introduced, 95.0% confidence intervals (CIs) were calculated using an unpaired two-tailed Poisson distribution. Incidence density rates for HO bacteremia and HO UTIs were calculated as the total number of infections per the total number of patient-days per 100,000 patient-days. Patient-days were calculated as the sum of the lengths of stay for all admissions in a given year. Incidence density rates for device-associated infections (CLABSIs and VAP) were calculated as the total number of infections per 100,000 device-days. Device-days were estimated as the sum of the lengths of stay for all admissions that indicated the use of the device of interest (central line or ventilator) during the admission. SSI rates were determined by dividing the number of SSIs by the sum of all surgical procedures performed in 2013. Rates were only calculated if the total number of infections was greater than or equal to five.[22]

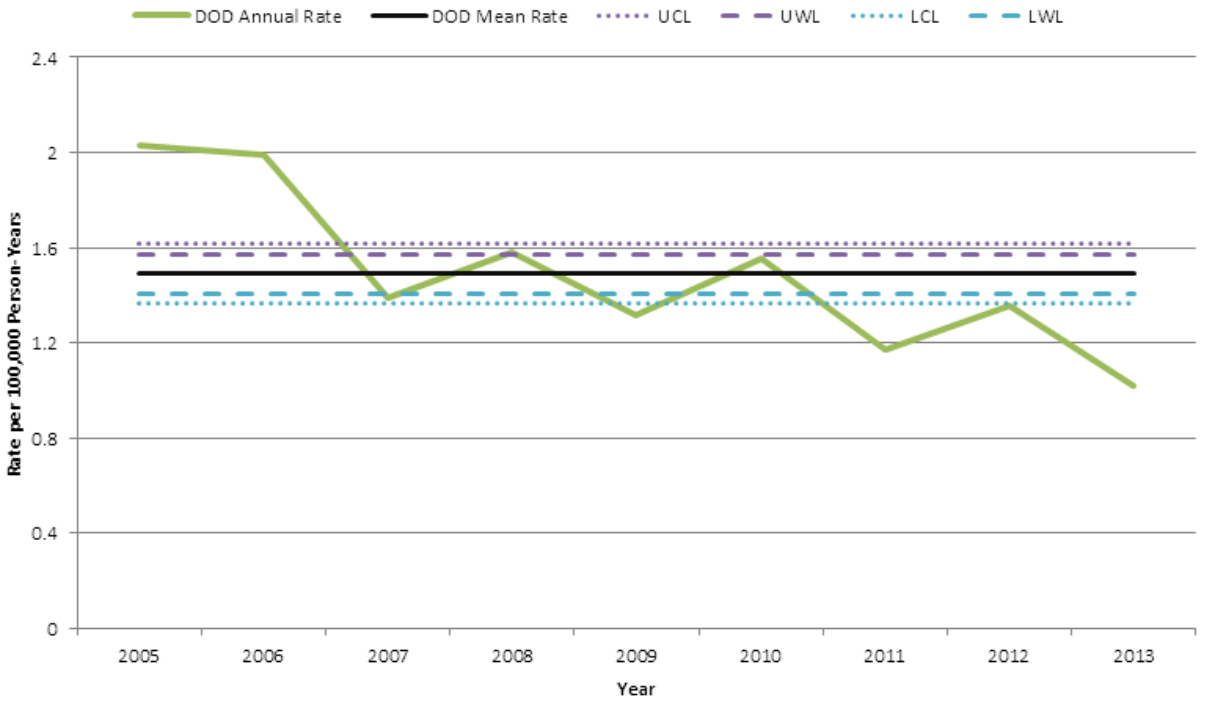
The statistical process control (SPC) was used to evaluate the statistical variation of VRE infection occurrences over the surveillance period. The mean incidence rates for the DOD and DON were calculated as the average infection rate from the eight-year period (2005-2012). The MHS Mart (M2) eligible beneficiary counts for the month of July of each year were used as a proxy for the average beneficiary count for that entire year. This proxy was also used as a denominator for calculating rates. Upper and lower warning limits (UWL, LWL) and upper

and lower control limits (UCL, LCL) were calculated using two standard deviations above (UWL) or below (LWL) the mean rate, and the UCL and LCL were calculated using three standard deviations above (UCL) or below (LCL) the mean rate.[24] Demographic rates were also calculated using the M2 July/yearly counts as the denominator. All rates are presented per 100,000 beneficiaries, unless otherwise specified.

Results

In CY 2013, the annual incidence rate of VRE infection for the DOD beneficiary population was 1.0 per 100,000 person-years. Overall, the VRE incidence rate has decreased since 2005. The DOD VRE incidence rate for CY 2013 was well below the DOD mean rate at 1.5 per 100,000 person-years. The incidence rate has remained below the LCL from 2011, when it fell outside the natural variation, through 2013 (Figure 1).

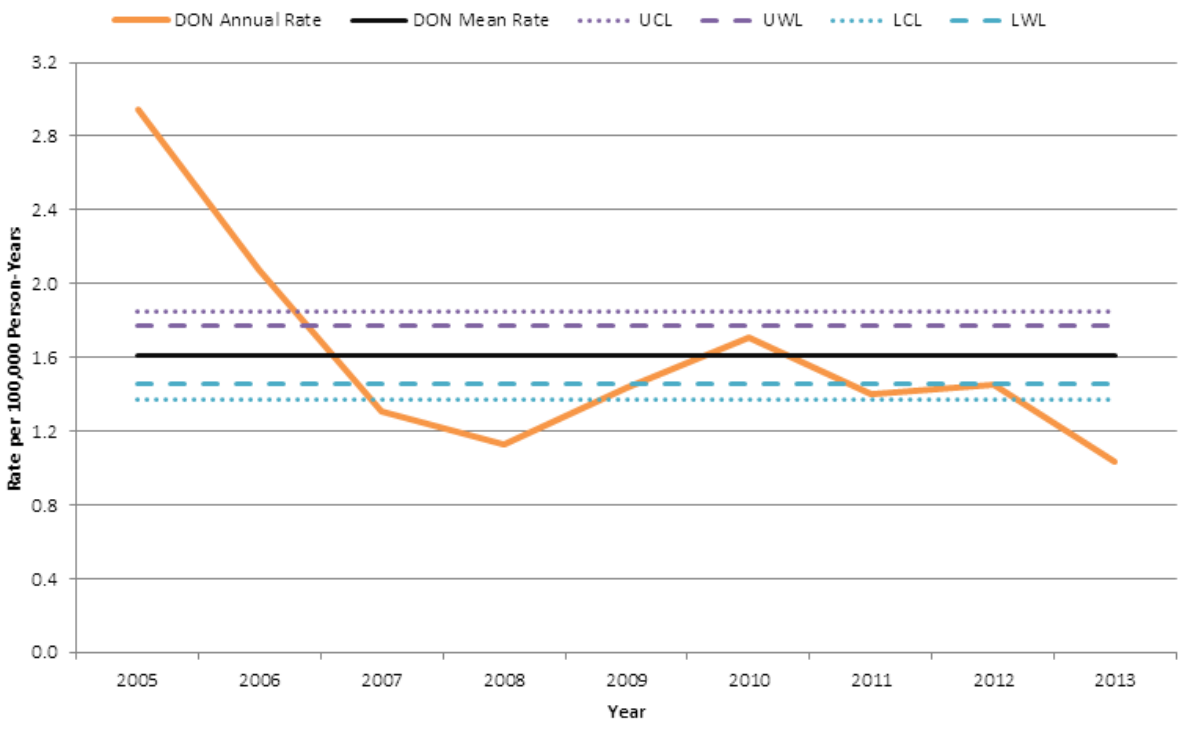
Figure 1. VRE Incidence Rates[a] among Department of Defense Beneficiaries, CY 2005 - 2013



[a]Incidence was identified as the first VRE isolate per person per year.
DOD mean rate calculated from 2005 - 2013 was 1.5 cases per 100,000 person-years.
Data source: Navy and Marine Corps Public Health Center Health Level 7(HL7) formatted microbiology data and MHS Mart (M2) data.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 2 June 2014.

The DON annual incidence rate for VRE infection in CY 2013 was also 1.0 per 100,000 person-years. There has been a decrease in VRE incidence in the DON since 2005, with the exception of a peak in 2010. Much like the DOD, the 2013 annual incidence rate is much lower than the mean rate, which is 1.6 per 100,000 person-years. The 2013 DON VRE incidence rate is also much lower than the LCL and well below natural variation.

Figure 2. VRE Incidence Rates[a] among Department of the Navy Beneficiaries, CY 2005 - 2013



[a]Incidence was identified as the first VRE isolate per person per year.
DON historic mean calculated from 2005 - 2013 as 1.6 cases per 100,000 person-years.
Data source: Navy and Marine Corps Public Health Center Health Level 7(HL7) formatted microbiology data and MHS Mart (M2) data.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 2 June 2014.

In CY 2013, there were 104 cases of VRE infection in the DOD. Of those, 34 (32.7%) were among DON beneficiaries (Table 2). For both the DOD and DON in CY 2013, higher rates of infections occurred among female beneficiaries and individuals aged 65 years or older. This pattern also occurred for previous years, 2005 to 2012. Higher rates for the DOD occurred in the West TRICARE region for 2013 and in the North TRICARE region historically, while the highest DON rates occurred in the West TRICARE region both in 2013 and historically (Table 2). In 2013, the highest rate of infection in the DOD sponsor services was among Navy beneficiaries at 1.4 per 100,000 eligible beneficiaries, while historically, the highest rate of infection was among the Air Force at 2.3 per 100,000 beneficiaries. For 2013, the Retired beneficiary category had the highest rate in the DOD and DON (Table 2). Historically, the Other beneficiary category had the higher calculated rates for the DOD and DON, but this is most likely due to the lower M2 denominators for that beneficiary category and the low annual VRE prevalence for each year (less than nine cases a year).

Table 2. Demographic Description of VRE Prevalence Cases[a] Among DOD and DON Beneficiaries, CY 2005-2013

	DOD				DON			
	2013 (N =104)		Historic[b] (N=1,401)		2013 (N = 34)		Historic[b] (N=443)	
	Count	Rate[c]	Count	Rate[c]	Count	Rate[c]	Count	Rate[c]
Gender								
Female	56	1.2	733	2.0	17	1.3	244	2.3
Male	48	1.0	668	1.8	17	1.2	199	1.8
Age Group								
0-17 years[d]	5	0.3	65	0.4	1	--	29	0.6
18-24 years[d]	5	0.4	110	1.1	4	--	46	1.3
25-34 years[d]	6	0.5	107	1.2	3	--	38	1.4
35-44 years[d]	5	0.6	87	1.2	1	--	46	2.1
45-64 years	24	1.1	389	2.3	9	1.4	106	2.1
65+ years	59	2.9	643	4.2	16	2.8	178	4.2
Sponsor Service								
Air Force	24	0.9	476	2.3				
Army	46	1.2	482	1.6				
Marine Corps	6	0.8	98	1.7	6	0.8	98	1.7
Navy	28	1.4	345	2.0	28	1.4	345	2.0
Beneficiary Type								
Active Duty	8	0.6	144	1.3	5	1.0	69	1.6
Recruit[d]	0	--	4	--	0	--	4	--
Family Member	55	1.0	748	1.8	16	1.0	253	2.1
Retired	41	2.0	472	2.9	13	2.1	107	1.7
Other	0	--	33	16.0	0	--	10	16.4
TRICARE Region								
Alaska[d]	0	--	2	--	0	--	0	--
North	37	1.3	532	2.3	14	1.4	175	2.1
OCONUS[d]	3	--	22	0.6	1	--	10	1.2
South	16	0.5	406	1.7	0	--	38	0.7
West	47	1.7	437	2.0	19	2.1	220	2.9
Unknown[d]	1	--	2	--	0	--	0	--

[a]Prevalence was identified as the first VRE isolate per person per calender month.

[b]Historic data are cumulative counts and rates from 2005-2012.

[c]Rates calculated per 100,000 beneficiaries.

[d]Rates are only presented if the count is higher than five.

[e]TRICARE service region cannot be determined from the microbiology data.

Data source: Navy and Marine Corps Public Health Center Health Level 7 (HL7) formatted microbiology data.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 9 May 2014.

Concerning clinical characteristics of the VRE infections within the DOD and DON in CY 2013, the majority of VRE infections identified were found in the inpatient setting, classified as HA, and diagnosed as UTIs (Table 3). For 2013, within the DOD, *E. faecium* caused 50.0% of VRE infections, while an unspecified *Enterococcus* species caused 52.9% of infections in the DON. Only a small number of VRE infections were classified as HO VRE for the DOD and the DON, which accounted for 7.7% and 6.5% of VRE infections, respectively (Table 3). Findings from 2013 are similar to historical trends from 2005 to 2012 for both the DOD and DON.

Table 3. Clinical Characteristics of VRE Prevalence Cases[a] among DOD and DON Beneficiaries, CY 2005-2013

	DOD				DON			
	2013 (N =104)		Historic[b] (N=1,401)		2013 (N = 34)		Historic[b] (N=443)	
	Count	Percent	Count	Percent	Count	Percent	Count	Percent
Encounter Type								
Inpatient	60	57.7	933	66.6	22	64.7	301	67.9
Outpatient	44	42.3	468	33.4	12	35.3	142	32.1
Healthcare[c]/Community Associated[c]								
Hospital-onset (H0)	8	7.7	102	7.3	3	8.8	29	6.5
Healthcare associated (HA)	40	38.5	496	35.4	17	50.0	152	34.3
Community-onset (CO)	37	35.6	445	31.8	14	41.2	140	31.6
Infection Type								
Urinary Tract	56	53.8	607	43.3	14	41.2	167	37.7
Blood Stream	14	13.5	265	18.9	6	17.6	81	18.3
Gastrointestinal Tract	3	2.9	67	4.8	0	--	41	9.3
Surgery	5	4.8	37	2.6	1	2.9	12	2.7
Skin and Soft Tissue	18	17.3	151	10.8	8	23.5	69	15.6
Respiratory	0	--	31	2.2	0	--	12	2.7
Sterile	2	1.9	29	2.1	2	5.9	14	3.2
Other	5	4.8	186	13.3	3	8.8	39	8.8
Species								
Enterococcus sp. unspec.	24	23.1	523	37.3	18	52.9	224	50.6
E. faecalis	15	14.4	147	10.5	4	11.8	47	10.6
E. faecium	52	50.0	627	44.8	11	32.4	147	33.2
E. gallinarum	7	6.7	54	3.9	1	2.9	13	2.9
E. casseliflavus	6	5.8	39	2.8	0	--	7	1.6
E. durans	0	--	5	0.4	0	--	2	0.5
E. raffinosus	0	--	5	0.4	0	--	2	0.5

[a]Prevalence was identified as the first VRE isolate per person per calender month.

[b]Historic data are cumulative counts and rates from 2005-2012.

[c]A VRE isolate can be classified as more than one healthcare or community associated exposure, therefore the counts may be greater than the total N.

Data source: Navy and Marine Corps Public Health Center Health Level 7 (HL7) formatted microbiology data and Standard Inpatient Data Record (SIDR).

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 9 May 2014.

Table 4 presents an antibiogram for the VRE isolates identified in the DOD from 2005 to 2013. There are a few instances where the numbers of isolates tested were less than 30, and those values should be considered with caution. VRE isolates among DOD beneficiaries in 2013 were most susceptible to linezolid and least susceptible to ciprofloxacin. Overall, the susceptibilities for the antibiotics evaluated remained stable over the surveillance period. Ampicillin, gentamicin-high, penicillin, and streptomycin-high had significant ascending trends during the surveillance period (*P*-value <.05), while tetracycline had a significant descending trend (*P*-value <0.0001). For the DON, the isolate counts were very low and would not support a meaningful antibiogram.

Table 4. Antibiogram of Vancomycin-Resistant *Enterococcus* species (VRE) Isolates Identified among the Department of Defense, CY 2005-2013[a]

Antibiotics	2005	2006	2007	2008	2009	2010	2011	2012	2013	*P*-value[b]
Ampicillin	15.7% 115	13.5% 104	15.9% 69	25.9% 81	25.3% 79	25.2% 119	23.8% 101	32.1% 109	35.4% 82	<0.0001
Ciprofloxacin	11.9% 84	6.7% 60	15.4% 39	4.4% 45	7.5% 53	8.8% 68	10.8% 37	4.2% 48	17.1% 35	0.9026
Daptomycin[c]	-- 0	100.0% 22	100.0% 10	100.0% 14	100.0% 13	100.0% 13	100.0% 10	100.0% 15	100.0% 16	N/A
Doxycycline[c]	85.7% 42	92.0% 25	75.0% 16	66.7% 12	75.0% 16	50.0% 20	33.3% 12	25.0% 8	33.3% 6	N/A
Erythromycin[c]	8.3% 12	0.0% 14	10.0% 10	7.7% 13	14.3% 14	16.7% 18	0.0% 11	0.0% 15	0.0% 5	N/A
Gentamicin-High	68.8% 96	68.2% 85	66.7% 75	69.3% 88	70.3% 74	62.5% 80	64.7% 68	78.1% 73	87.1% 62	0.0460
Levofloxacin[c]	29.2% 24	16.7% 48	30.4% 23	19.4% 31	8.3% 24	14.3% 35	11.8% 34	20.7% 29	25.0% 32	N/A
Linezolid[c]	92.0% 75	90.4% 73	90.9% 33	91.3% 46	95.5% 44	85.5% 55	88.2% 34	88.6% 35	92.9% 28	0.5815
Nitrofurantin	44.6% 56	58.5% 53	38.7% 31	46.2% 39	35.4% 48	33.9% 59	46.3% 41	44.2% 52	47.5% 40	0.4483
Penicillin	18.2% 43	15.3% 144	13.4% 82	21.0% 100	21.3% 89	20.8% 101	18.6% 70	21.4% 70	36.2% 58	0.0060
Quinupristin/Dalfopristin[c]	76.1% 71	85.7% 70	82.4% 34	73.8% 42	84.2% 38	81.0% 42	72.0% 25	85.7% 28	75.0% 20	N/A
Rifampin[c]	7.1% 56	16.7% 30	11.8% 17	25.0% 16	0.0% 21	14.8% 27	20.0% 15	14.3% 21	15.4% 13	N/A
Streptomycin-High	41.1% 112	46.2% 93	62.9% 70	64.0% 86	64.9% 74	64.6% 82	66.7% 66	73.8% 65	81.5% 54	<0.0001
Tetracycline	63.9% 97	61.2% 85	75.0% 48	58.1% 62	49.3% 69	35.3% 85	23.0% 61	22.4% 76	19.0% 58	<0.0001

[a]Only the first vancomycin-resistant *Enterococcus* species isolate per patient per calendar year were included; surveillance cultures was excluded.

[b]*P*-values were determined using the Cochrane-Armitage test for trend.

[c]Treat with caution if isolate counts are less than 30.

Top percent reflects the percent susceptible the VRE isolate counts were to that antibiotic.

Number below the percent susceptible is the total number of isolates tested against that antibiotic.

Data source: NMCPHC Health Level 7 (HL7) microbiology data.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 14 May 2014.

Table 5 displays the exposure burden for DOD and DON VRE HA infections. Both the admissions and overall prevalence rates for 2013 are lower than the calculated historic mean. The rate of VRE importation into fixed MTFs for 2013 was 14.0 per 100,000 admissions for the DOD and 16.0 per 100,000 admissions for the DON. The overall prevalence of VRE infections for the DOD and DON in 2013 were 18.0 per 100,000 admissions and 22.6 per 100,000 admissions, respectively. In comparison to the historical mean rates, the DOD and DON rates for 2013 are lower. In regards to infection burden, due to low case counts, the rates for HO bacteremia, HO UTIs, SSIs, CLABSIs, and VAP were not calculated for either the DOD or DON for the surveillance period.

Table 5. Overall Hospital-Acquired Infection Exposure Burden for Vancomycin-Resistant *Enterococcus* species Infections in the DOD and DON[a]

	DOD		DON	
	2013	Historic[b]	2013	Historic[b]
Exposure Burden	Overall Rate	Mean Rate (95% CI)[c]	Overall Rate	Mean Rate (95% CI)[c]
Overall	18.0	25.7 (16.6, 37.5)	22.6	25.3 (16.6, 37.5)
Admission	14.0	19.6 (11.8, 30.3)	16.0	20.2 (12.2, 30.9)

[a]Rates were calculated per 100,000 admissions
[b]Historic mean rates were calculated from the 2005-2012 rates for each parameter.
[c]95% confidence intervals were calculated based on Poisson distribution, two-tailed.
Data Source: NMCPHC Health Level 7 (HL7) microbiology and Standard Inpatient Data Record (SIDR) data.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 2 June 2014.

Discussion

Since 2005, the overall VRE incidence rate has been declining. This is true for the DOD and DON beneficiary population in 2013. The DOD and DON annual rates for 2013 were lower than the mean historical rate, by 0.5 (33.3%) and 0.6 (37.5%), respectively. These decreasing trends could be explained by awareness, infection control, and better antibiotic prescription practices being enforced and regulated.

Within the DOD and DON, demographic groups most impacted by VRE infections were people aged 65 or older, retired, Navy sponsors and beneficiaries located in the West TRICARE region. For the DOD, VRE infection rates were higher among females. VRE can colonize the genital tract in both females and males, however, females are more prone to UTIs than men, therefore, it is expected that females would be more likely to acquire infection than males.[26] Higher rates of VRE infection are also expected among people aged 65 or older. As a person ages, they are more likely to become ill and end up in the hospital where many of the VRE infections are acquired.[25]

Most VRE infections in 2013 occurred in the inpatient setting for the DOD and DON, and the majority of infections were classified as healthcare associated (DOD = 38.5%; DON = 50.0%). *Enterococcus* infections are more likely to occur among very sick patients in hospitals or other health-care settings. About 30% of *Enterococcus* health-care associated infections are vancomycin-resistant.[25] Hospital associated VRE infections pose a serious threat on ill

hospitalized patients, especially among patients with prolonged hospital stays. Unfortunately, the DOD and DON healthcare associated cases of VRE have increased by 3.1% and 15.6%, respectively, compared to the historic rates. A NHSN report showed that the percent of healthcare associated VRE infections decreased from 4.0% in 2006-2007 to 3.0% in 2009-2010.[25,26] Reports for healthcare associated VRE infections in the general population in 2013 are not readily available so a direct comparison to the DOD and DON is not currently possible. However, it is concerning that the rates of healthcare associated VRE infections among the DOD and DON have increased in the past year.

Classifications for healthcare associated VRE infections may overlap with community onset since healthcare associated classifications include patients with disease onset following recent exposures to healthcare delivery within the community. Although there is no community reservoir for VRE in the US, research has shown that patients can remain colonized for weeks or even months and are often still colonized at the time of readmission to the hospital.[8] This leads to potential VRE transmission within the community and healthcare facilities, especially long-term care facilities.

Whether VRE is acquired in the community or the hospital, VRE infections can still be treated with effective antibiotics. Over the surveillance period, linezolid susceptibility remained stable with an average of 92.9% susceptibility, indicating that VRE isolates remain highly susceptible to linezolid. Susceptibility for gentamicin, an antibiotic also recommended for VRE treatment, and streptomycin increased over the surveillance period and remains a viable treatment option. The availability of effective treatments is extremely important for treating VRE infections and preventing mortality and morbidity.

The admissions prevalence metric measures the magnitude of VRE imported into the healthcare system, and the overall prevalence rate measures the reservoir of infection in a healthcare setting.[22] Current infection control practices in the healthcare setting appears effective, as both exposure burden metrics for the DOD and DON in 2013 are lower than the calculated historic mean rate. This indicates that fewer people with VRE infections are being admitted to the hospital and that hospitals are decreasing patient's exposure to other patients with VRE. These are excellent methods to limit VRE exposure to high-risk populations such as the elderly, severely ill or long-term care patients.

Overall, the incidence rates of VRE in the general US population, the DOD and DON are decreasing. No substantial changes in VRE risk groups were seen for 2013 as VRE continues to affect elderly females and manifest as urinary tract infections. In addition, no substantial changes in antibiotic susceptibility were seen in 2013. Linezolid, gentamicin and streptomycin remain viable treatments for VRE. Although current infection control practices seem to be decreasing the overall burden of VRE, healthcare associated infections are still a major problem for transmission of VRE in the DOD and the DON. Better infection control practices need to be introduced to help control healthcare associated infections.

Limitations

HL7 data are generated within the Composite Health Care System (CHCS) at fixed MTFs. Microbiology testing results only report the organism(s) that were identified, not what the test was intended for (e.g., if a physician suspects an organism different from the one that was identified, the record will not show the organism that the physician suspected).

Microbiology data are useful for identifying laboratory-confirmed cases of illness. Laboratory-confirmed VRE specimens only indicate that a VRE was isolated, not that it is the primary cause of infection. Dual infections were not analyzed. Cases in which a physician chooses to treat presumptively without laboratory confirmation are not captured. Clinical practice with regards to culturing varies between providers and facilities. Examples of situations where cultures may not be performed include confirmatory tests for patients with influenza-like illness symptoms, or patients with superficial infections who are treated presumptively. Cases in which a physician chose to treat based on a positive surveillance culture are also not captured. Therefore, the isolate counts here are likely an underestimate of the actual VRE burden in the DOD and DON.

The use of microbiology data for analysis of antibiotic resistance is limited by the practice of cascade reporting, where antibiotic sensitivity results are conditionally reported to CHCS to guide treatment decisions. Cascade reporting is practiced to varying degrees at DOD MTFs. Non-standard test records are not be captured in the HL7 restructure process (e.g., when an organism or antibiotic names appear in the test result field). Thus, a complete picture of the susceptibility patterns for VRE isolates is not known, and the presumption of reduced susceptibility is applied to all antibiotics in a class if an isolate is shown to be resistant to that class. It is also important to note that DOD laboratories do not all use the same breakpoints to interpret susceptibility results, thus making MDRO identification subject to some inconsistency.

A SIDR is created at discharge or transfer from an inpatient MTF for all DOD beneficiaries. For active duty personnel, this occurs for non-military medical treatment facility discharges as well. For all other DOD beneficiaries, a SIDR is only created on discharge from a MTF. Patient encounter records depend on correct ICD-9-CM coding practices. Data for medical surveillance are considered provisional and medical case counts may change if the discharge record is edited after the patient is discharged from the MTF.

SIDR data are also limited in that it is difficult to associate a specific microbiology record with a procedure, particularly when a patient has multiple surgeries. If a specimen source was unspecified then the isolate could not be definitively linked to a procedure or device ICD-9-CM code. This potentially makes the SSI rate an overestimate. In addition, if an individual underwent multiple surgeries it was difficult to attribute a positive VRE specimen to a single surgery as the procedure dates do not appear reliably in the data. Also, the values used to calculate the metric density-rate for SSIs and VAP respectively are very small due to low numbers of infections identified in these categories. These results should therefore be considered with caution.

It is possible that not all antibiotic prescriptions were dispensed in response to a VRE infection.

Antibiotics that were prescribed within the appropriate timeframe to be associated with a VRE specimen collection date may have been provided for reasons other than the VRE infection, such as a different infection occurring after the VRE species was isolated. However, most antibiotics identified as being associated with a VRE infection were antibiotics that are typically used to treat VRE, and therefore likely that the majority of prescriptions in this analysis were truly in response to VRE infections.

Cases where a physician chose to treat presumptively were not captured as HL7 microbiology records. As only VRE isolates were identified, it is unknown if patients had a concurrent infection with another organism that a prescribed antibiotic could have alternatively been intended for. However, the majority of antibiotics prescribed were antibiotics that could be used in the treatment of a VRE infection, leading one to believe VRE was the intended target for the antibiotic prescription.

All the above mentioned databases are limited in that they do not include data from purchased care, shipboard facilities, battalion aid stations, or in-theater facilities. Therefore, these results are only an estimate of the true VRE infection burden in the DOD and DON. In an effort to account for data lag and capture all finalized records from 2013, data were pulled after a waiting period of four months (data pulled April 2014). The majority of records used in this analysis are presumed with some certainty to be final, but there is the possibility that some records were updated after the data were pooled.

Acknowledgements

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